

**STUDY ON CHRONIC PANCREATITIS
AT GOVERNMENT RAJAJI HOSPITAL, MADURAI**

**DISSERTATION SUBMITTED FOR
BRANCH - I M.S., (GENERAL SURGERY)**

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CHENNAI**

BONAFIDE CERTIFICATE

This is to certify that the dissertation entitled “ **STUDY ON CHRONIC PANCREATITIS AT GOVT. RAJAJI HOSPITAL, MADURAI** ” submitted by **Dr. M. SIVAKUMAR** to the Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the requirement for the award of M.S Degree Branch – I (General Surgery) is a bonafide research work were carried out by him under direct supervision & guidance.

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This is submitted to The Tamilnadu Dr. M. G. R. Medical University, Chennai in partial fulfillment of the rules and regulations for the M.S degree examination in General Surgery.

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INTRODUCTION

Chronic pancreatitis is a relentlessly progressive fibroinflammatory process, resulting in various amounts of destruction of endocrine and exocrine elements, which may eventually lead to pancreatic insufficiency.

Abdominal pain which is excruciating and recurrent is dominant feature of chronic pancreatitis that initially brings most of the patients to physician's attention. The pathogenesis of pancreatic pain is often multifactorial and explains why not all patients respond to same mode of therapy.

In contrast to the quantitatively huge interest stands. The fact that basic problem concerning the disease, the initial steps, the propagation, the mechanisms are still unsolved. This obvious defect in knowledge and understanding of what really going on, when individual get a chronic pancreatitis bears a profound influence on therapeutic approach to the disease.

AIM OF THE STUDY

1. To study the epidemiological patterns in relation to age, sex and place.
2. To study the different etiological factors and pattern of clinical presentations.
3. To study the incidence of the Chronic pancreatitis at GRH, Madurai
4. To know the outcome and response of the surgical drainage procedure.

REVIEW OF LITERATURE

1. **Surgical management of chronic pancreatitis : Long term result in 141**

patient. Br.J. Surg 1988.

Mannell A ; Adson MA ; McIlrath DC ; Ilstrup DM ; Department of Surgery Mayo Clinic Rochester, Minnesota

- 141 patient were operated for chronic pancreatitis at Mayo clinic. The main indication was pancreatic pain and choice of operation was based on anatomical abnormalities in the gland.
 - Mean follow up period – 8.5 years
 - Number of patient operated – 141 patients
 - **Conclusion**
 - 77% of operated patient had lasting pain relief
 - Longitudinal pancreatico jejunostomy in those with dilated duct and whipple operation for disease of pancreatic head gave good results.
- 2. Local resection of the head of the pancreas combined with longitudinal pancreatico-jejunostomy in the management of patients with chronic pancreatitis.**

Ann Surg 1994, Frey CF : Amikura K, Department of Surgery, University of California, Davis Medical Centre, Sacramento.

Material -The operation was performed on 50 patients, pain relief, endocrine and exocrine insufficiency and weight gain were assessed.

Conclusion - The LR – LPJ provides good pain relief with modest increase in endocrine and exocrine insufficiency and a significant increase in weight. Even when relieved of pain, patients seldom return to the work force.

3. Pain relapse in the first 10 years of chronic pancreatitis, An. J Surg 1996.

**Talamani G ; Bassi C, Falconi ; Sartorin ; Salvia R ; DiFrancesco V ;
Frulloni L ; Vaona B ; Bovo P ; Vantin I ; Pederzoli P ; Cavallini G.
Department of Medicine University of Verona, Italy.**

To evaluate whether the annual number of pain relapse of chronic pancreatitis correlated with sex, type of pancreatitis, drinking and smoking and type of surgery .

Length of follow up - 10 yrs

Number of patients - 2,034 / year

Conclusion - Regardless of surgical treatment patients should be advised to reduce both their alcohol intake and cigarette smoking.

4. Chronic Pancreatitis, Paul Georg Lankisch MD, sur Opin Gastroenterology 2007.

Abstract : Purpose of Review is to focuss on the most important new observations in chronic pancreatitis.

Recent findings –

- Superiority of Surgery compared with endotherapy for long term pain relief.

- Smoking enhances the risk of chronic pancreatitis
- New insights in Autoimmune pancreatitis

Study :

Amsterdam group conducted Randomized trial, Comparing endoscopic and surgical drainage of the pancreatic duct.

39 - patients participated

19 – endoscopic treatment

20 – surgical drainage procedure

Follow up period – 24 months

Result :

Complete or partial pain relief

32% - Endoscopic group

75% - Surgery group

5. Surgical Management of CP:

Gourgiotis S,

Germanos S, Ridolfini MP, Department of hepatobiliary and pancreatic surgery. Royal London Hospital London, UK. Hepatobiliary pancreatic Dis

Int 2007 Apr 6.

Background :

During the last

decade increasing knowledge about pathophysiology of CP, improved results of major pancreatic resections and integration of sophisticated diagnostic methods in clinical practice resulted in significant changes in surgery for CP.

Conclusion :

Surgical procedure

provide long term pain relief a good post operative quality of life with preservation of endocrine and exocrine function. In addition to available results from randomized controlled trials, new studies are needed to determine which procedure is most effective for the management of patient with CP.

6. Extended drainage versus resection in Surgery for CP : A prospective randomized trial comparing LPJ + Local pancreatic head excision with pylons preserving pancreatoduodenectomy.

Ann Surg 1998, Dec, Izbicki JR, Bloechle C, Broering DC, Knoefel WT, Kuechler T, Broelsch CI. Department of Surgery University of Hamburg, Germany.

To analyse the efficacy of LPJ – LPHI & PPPD

Number of patients – 61 patients were randomly allocated

Conclusion: – Both procedures are equally effective in terms of pain relief and definitive control of complications affecting adjacent organ, but extended drainage procedure provides better quality of life.

7. Comparative RCT between endoscopic treatment with surgical treatment in painful obstructive CP. Dite et al, Endoscopy 2003.

Number of patients - 140

Surgery - 80% Resection, 20% drainage

Endoscopy – 52% sphincterotomy and

Stenting, 23% stone removal,

Follow up period – 5 yrs

Conclusion :

Pain relief after surgery is superior to endotherapy in patient with painful obstructive CP.

8. Chronic pancreatitis : A prospective nationwide study of 1086 subjects from India

Balakrishnan V, Unnikrishnan AG, Thomas V, Choidhini Veera raju P, Singh IP, Garg P, Pai CG, Devi RN, Bhasin D, Jayanthi D, Premalatha N, Chacko A..., Amitha Institute of Medical Science, Cochin India, Sep 2008 : pub Med.

Study : Prospective nationwide study of risk factors and clinical profile of Chronic pancreatitis

Setting : 32 major centres from all over India contributed data on 1,086 patients.

Outcome Measures : Risk factors, Clinical features, complications and treatment of Chronic pancreatitis.

Conclusion : In this first nationwide prospective study of Chronic pancreatitis in India, Idiopathic Chronic pancreatitis was the most common form, followed by

alcoholic pancreatitis. The classical form of tropical Chronic pancreatitis is becoming less common.

9. Comparative study of the clinical profiles of Alcoholic chronic pancreatitis and tropical Chronic pancreatitis in Tamilnadu, South India.

Chari ST, Mohan V, Jeyanth V, Snehalatha C, Malathis, Viswanathan M, Madanagopalan N. Department of Digestive Health and Disease Government Peripheral Hospital, Madras, India Pub Med : Pancreas : 1992.

Number of patients - 50

Conclusion : TCP and ACP have distinct clinical profile and it is possible that some environments factors may hasten the progress of ACP in the tropics.

HISTORY OF PANCREATIC ANATOMY

The pancreas was first mentioned in the writing of Eristratos (310-250 BC) and given its name by Rufus of Ephesus (Crica 1040). The name pancreas (Greak Pan-

all, kreas-flesh almost) was used because the organ contain neither cartilage or bone. Its main duct was described by Wirsung in 1642, where the enlargement of the duct at its junction with the CBD and its projection in to the duodenum as a papilla were first described by Vater in 1720. Santorini in 1734 described the accessory duct that bears his name. It was only after demonstration of digestive enzymes by Claude Bernard in 1850 that the pancreas became a complete organ with an important function and thus a worthy object of study.

Inspite of the apparent accessibility of the pancreas, a number of complex relations combines to make its surgical removal difficult. In 1899 Halsted was first to successfully remove the head of pancreas and portion of duodenum for ampullary carcinoma. Several surgeons developed two staged operations, for removal of head of pancreas. These efforts culminated in 1940 with one stage operation of whipple.

Sir Andrew Watt kay wrote in 1978, “For me, the tiger country is removal of the pancreas. The anatomy is very complex and one counters anomalies”.

Location :

The pancreas lies posterior to the stomach and lesser omentum in the retroperitoneum of the upper abdomen. It extends obliquely rising slightly as it passes from the medial edge of duodenal C loop to the hilum of the spleen. It lies anterior to the inferior venacava, aorta, splenic vein and left adrenal gland.

Regions :

Pancreas is divided into four regions. The head and uncinate process, neck, body and tail. The head lies within the duodenal loop and its uncinate process extends posteriorly and medially to lie behind the Superior mesenteric vein and SMA. The neck of the gland extends medially from the head to lie anterior to these vessels. The body extends laterally from the neck toward the spleen, where as the tail extends into the splenic hilum.

Blood supply and Lymphnodes :

Both the celiac trunk and the SMA provide the arterial supply to the pancreas. Variations are common, but for the most part, the body and tail are supplied by branch of the splenic artery, where as head and uncinate process receive their supply through arcade originating from the hepatic and gastroduodenal branch of celiac artery and from the first branch of the SMA.

Venous drainage is to the splenic vein, SMV and portal vein. The pancreas is drained by multiple lymph node groups. The major drainage of pancreatic head and uncinate process is to the subpyloric, portal, mesenteric, mesocolic and aortocaval node. The pancreatic body and tail for the most part are drained through nodes in the celiac, aortocaval, mesenteric and mesocolic groups and through nodes in the splenic hilum.

Innervation :

The pancreas is innervated by both sympathetic and para sympathetic components of the autonomic nervous system. The principal and possibly only, pathway for pancreatic pain involves nociceptive fibers arising in the pancreas. They pass through the celiac ganglia to form the greater, lesser and least splanchnic nerves that pass to cell bodies in the thoracic sympathetic chain. Efferent visceral motor supply to the pancreas is provided by both the sympathetic and parasympathetic systems. The latter involves preganglionic fibers arising from cell bodies in the vagal nuclei that travel through the posterior vagal trunk to the celiac plexus. Postganglionic fibers then innervate pancreatic islets, acini, ducts and blood vessels. In general, the nerves of the pancreas travel with the blood vessels supplying the organ.

Ducts :

The main pancreatic duct, or duct of Wirsung arising in the tail of the pancreas and terminates at the papilla of Vater in the duodenum. It crosses the vertebral column between T12 and L2. Within the body and tail of the pancreas, the duct lies slightly caphaled to a line drawn midway between the superior and inferior edges. The duct is also more posterior than anterior. In adults, the duct within the head measures 3.1 to 4.8 mm in diameter and gradually tapers to measure 0.9 to 2.4 mm in the tail. With age, the duct diameter can increase. The duct of Santorini ie. the minor or accessory pancreatic duct is smaller than the

main duct. It extends from the main duct to enter the duodenum at the lesser papilla. That Papilla lies about 2 cm proximal and slightly anterior to the major papilla.

EMBRYOLOGY

Organogenesis :

During the 4th week of gestation, two endodermal buds arise from the duodenum ; the hepatic diverticulum, which is destined to form the liver, gall bladder and bile ducts, and the dorsal pancreatic bud that forms the body and tail of the pancreas. On the 32nd day of gestation, this hepatic diverticulum gives rise to a ventral pancreatic bud that eventually develops into the uncinat process and inferior part of the head of the pancreas. The dorsal pancreatic bud extends transversely across the abdomen to lie anterior to the portal and mesenteric vessels. With time and as the duodenum rotates to form a C loop configuration the ventral pancreas and distal bile duct undergo clockwise rotation around the back of duodenum to finally, lie on the medial side of the duodenum, inferior and slightly posterior to the dorsal pancreas and posterior to the portal and mesenteric vessels. On the 37th day of gestation, the two pancreatic buds fuse and in 90% of individuals, their duct system also join.

HISTOLOGY

The mature pancreas is an endocrine organ made up of the islets of Langerhans and an exocrine organ consisting of acinar and ductal cells. The acinar cells, so named because they are clustered like grapes on the stem of a vine, discharge their secretions into a centrally located acinar space that communicates with the major pancreatic duct. Most of the cells in the pancreas are acinar cells and duct cells make up only 5% of pancreatic mass. Histologically, acinar cells have a high content of endoplasmic reticulum and an abundance of apically located eosinophilic zymogen granules. The cells lining the main pancreatic duct are tall columnar cells and many contain mucin granules. With progression from the large ducts to the smaller intralobular and interlobular ducts the lining cells become flatter, assuming a cuboidal configuration, and the mucin granules are no longer seen. Centroacinar cells located at the junction between ducts and acini resemble acinar cells in size and shape but lack zymogen granules.

PHYSIOLOGY

About 2.5 liters of clear, colorless, bicarbonate-rich pancreatic juice, containing 6 to 20g of protein, is secreted by the human pancreas each day. It plays a critical role in duodenal alkalization and in food digestion.

Protein Secretion :

With the possible exception of the lactating mammary gland, the exocrine pancreas synthesizes protein at a greater rate, per gram of tissue, than any other organ. More than 90% of that protein consists of digestive enzymes. Most of the digestive enzymes are synthesized and secreted by acinar cells as inactive proenzymes or zymogens that, in health, are activated only after they reach the duodenum where enterokinase activates trypsinogen and the trypsin catalyses the activation of the other zymogens. Some of the pancreatic digestive enzymes are synthesized and secreted in their active forms without the need for an activation step (eg. Amylase, lipase, ribonuclease). Acinar cells also synthesize proteins, including enzymes, that are not destined for secretion but, rather, are intended for use within the acinar cell itself. Examples of this latter group of proteins include the various structural proteins and lysosomal hydrolases.

Newly synthesized proteins are assembled within the cisternae of the rough endoplasmic reticulum and transported to the Golgi, where they are modified by

glycosylation. Those destined for secretion pass through the Golgi stacks and are packaged within condensing vacuoles that evolve into zymogen granules as they migrate toward the luminal surface of the acinar cell. By a process involving membrane fusion and fission, the contents of the zymogen granules are then released into the acinar lumen. Other proteins that are not destined for secretion are segregated away from the secretory pathway as they pass through the Golgi, and they are then targeted to their appropriate intracellular site.

Secretion of protein from acinar cells is a regulated process. At rest, secretion occurs at a low or basal rate, but this rate can be markedly increased by secretory stimulation that, in the pancreas, is both hormonal and neural. Pancreatic acinar cells can express receptors for acetylcholine. Cholecystokinin, secretin, and vasoactive intestinal peptide. Stimulation of secretion by either acetylcholine or cholecystokinin has been shown to involve activation of phospholipase C, generation of inositol triphosphate and diacyl glycerol, and a rise in intracellular ionized calcium levels that, by yet unidentified mechanisms, upregulates the rate of secretory protein discharge at the apical cell membrane. In contrast, secretin and vasoactive intestinal peptide activate adenylate cyclase, increase cellular levels of cyclic adenosine monophosphate (AMP), and activate protein kinase A. This also leads to protein secretion at the apical pole. Recent studies indicate that human acinar cells may not possess receptors for

cholecystokinin and that , in humans, cholecystokinin stimulation of secretion is mediated by intrapancreatic nerves that express cholecystokinin receptors.

Electrolyte Secretion :

Although stimulation of acinar cells results in the secretion of a small amount of serum like fluid, most of the fluid and electrolytes secreted from the pancreas arise from duct cells. The earliest step in duct cell electrolyte secretion involves diffusion of circulating carbon dioxide into the duct cell, and that carbon dioxide is hydrated by carbonic anhydrase to yield carbonic acid. Subsequently, the carbonic acid dissociates into protons and bicarbonates ions. The protons diffuse out of the cell and are carried away in the circulation while the bicarbonate remains inside the cell. The fluid and electrolyte secretagogue secretion acts, through a cyclic AMP mediated process, to stimulate chloride secretion, at the apical cell surface, through cystic fibrosis transmembrane regulator (chloride) channels. Then, through an apical chloride-bicarbonate exchanger, the actively secreted chloride is taken up again by the duct cell in exchange for bicarbonate. Taken together the result of these events is the secretion of a bicarbonate rich fluid into the duct and the discharge, into the circulation, of protons. In the absence of secretin stimulation, pancreatic juice has a more plasma like composition because it is composed primarily of acinar cell secretions and there is little duct cell secretion of chloride to permit exchange with bicarbonate. With secretin

stimulation, chloride secretion is increased, flow rates rise, and chloride bicarbonate exchange results in juice that is rich in bicarbonate and poor in chloride.

Integrated Physiology :

During the resting (interdigestive) phase of gastrointestinal function, pancreatic secretion is minimal and may be as low as 2% of that noted with maximal stimulation. The pancreatic response to a meal is a three phase process that includes a cephalic phase, a gastric phase, and an intestinal phase. The cephalic phase, accounting for 10% to 15% of meal stimulated pancreatic secretion, reflects the response to the sight, smell, or taste of food. It is believed to be almost exclusively mediated by peripherally released acetylcholine, which directly stimulates pancreatic secretion of enzymes and gastric secretion of acid. The acid indirectly stimulates pancreatic secretion of fluid and electrolytes by causing duodenal acidification and secretin release. The gastric phase of pancreatic secretion, accounting for 10% to 15% of meal-stimulated pancreatic secretion reflects the response to gastric distention and the entry of food into the stomach. These events can cause release of gastrin and stimulate vagal afferents. By binding to cholecystikinin receptors, gastrin is itself a weak stimulant of pancreatic enzyme secretion. Vagal stimulation also increases enzyme secretion.

More important, however gastrin and vagal stimulation cause gastric acid

secretion, and this leads to duodenal acidification, release of secretin from the duodenum, and pancreatic secretion of fluid and electrolytes. The intestinal phase of pancreatic secretion reflects the response to food and gastric secretions entering the proximal intestine. Acidification of the duodenum and the presence of bile in the duodenum promote secretin release. In addition, in the duodenum and proximal small intestine, the presence of fat and protein, as well as their partial breakdown products, stimulates the release of cholecystokinin, and this cholecystokinin stimulates enzyme secretion from acinar cells. The intestinal phase of pancreatic secretion accounts for 70% to 75% of meal stimulated pancreatic secretion.

ETIOLOGY OF CHRONIC PANCREATITIS

Newer classification systems, such as the TIGAR-O, categorize chronic pancreatitis based on the various known etiologic factors and mechanisms that are jointly considered risk modifiers (TIGAR-O) toxic, metabolic, idiopathic, genetic, autoimmune, recurrent severe, obstructive.

We discuss the various causes of chronic pancreatitis based on the TIGAR-O system.

Multiple toxic and metabolic etiologies involved in chronic pancreatitis. The association of alcohol and chronic pancreatitis was first described by COMFORT and associates in 1946. Alcohol is still the most common cause of chronic pancreatitis in Western industrialized countries, but only 5% to 10% of alcoholics develop clinically apparent chronic pancreatitis, and at autopsy 10% to 20% of alcoholics are found to have evidence of chronic pancreatitis.

Because only a fraction of alcoholics develop chronic pancreatitis, involvements of other factors are actively being investigated. Several evidence have shown that in addition to direct effects of alcohol, various predisposing factors, including genetics, smoking, intestinal infection, high fat diet, compromised immune function, gallstones, gender, hormonal factors and drinking patterns may render the pancreas more susceptible to alcohol induced tissue injury.

Smoking also is independently associated with increased risk for chronic pancreatitis. Chronic pancreatitis induced by smoking is particularly associated with pancreatic calcification. By mechanisms similar to alcohol, tobacco produces alterations in the secretion and composition of pancreatic juice mainly as a result of decreased pancreatic juice and bicarbonate secretion and induction of oxidative stress.

Calcium plays a central role in trypsinogen secretion and trypsin stabilization. Hypercalcemia caused by primary or secondary hyperparathyroidism results in recurrent acute pancreatitis, which progresses to chronic pancreatitis, likely owing to trypsinogen activation, which results in necrosis and fibrosis of the parenchyma.

Increased serum calcium concentration is believed to induce direct damage to acinar cells, and increased secretion of calcium results in intraductal stone formation. Hypercalcemia also seems to modify pancreatic secretion, leading to protein plug formation.

Idiopathic :

Thirty percent of patients with chronic pancreatitis do not have known risk factors for chronic pancreatitis and are considered to have idiopathic pancreatitis. Mutations of the serine protease inhibitor, Kazal type 1 (spink 1) gene in 25% of patients with idiopathic chronic pancreatitis. Based on the bimodal age of onset

of the clinical symptoms, idiopathic pancreatitis is separated into two distinct entities. Early onset idiopathic chronic pancreatitis presents during the first 2 decades of life with abdominal pain being the predominant clinical feature, whereas pancreatic calcifications and exocrine and endocrine pancreatic insufficiency are rare at the time of first diagnosis.

In contrast, the clinical presentation of late onset idiopathic chronic pancreatitis is in patients in their 40s, usually following a rather painless course, but associated with significant exocrine and endocrine pancreatic insufficiency and pancreatic calcifications.

Tropical or nutritional pancreatitis is considered a form of idiopathic chronic pancreatitis. It is the most common form of chronic pancreatitis in certain parts of the world, such as **India**, sub-Saharan Africa, and Brazil, and affects children and young adults (Schneider et al 2002). The disease is subdivided into tropical calcific pancreatitis, which is characterized by severe recurrent and chronic abnormal pain and extensive pancreatic calcifications, and fibrocalculous pancreatic diabetes, which is characterized by significant pancreatic endocrine insufficiency. This form of chronic pancreatitis is related to mutations in the SPINK 1 gene.

Strong association between cystic fibrosis transmembrane conductance regular (CFTR) mutations and idiopathic chronic pancreatitis. One third of all

patients with idiopathic chronic pancreatitis have CFTR mutations.

Leading pancreatologists speculate that most chronic pancreatitis might be a genetic disease with multifactorial triggering factors.

Genetic :

Until more recently few data existed on the genetic basis of chronic pancreatitis. The only known hereditary form of chronic pancreatic insufficiency that was well studied was cystic fibrosis.

Research has focused on the SPINK1-N34S gene mutation, which also is associated closely with tropical (50%), alcoholic (6%), or idiopathic (20%) chronic pancreatitis.

One of the major discoveries in chronic pancreatitis was the description of the point mutation in patients with autosomal dominant hereditary pancreatitis. Several variants of the mutation of the cationic trypsinogen gene all lead to a malfunction of trypsinogen. Hereditary pancreatitis presents typically in a bimodal pattern of childhood and adulthood. Hereditary pancreatitis is an autosomal dominant disease associated with trypsinogen gene mutations that carries an 80% penetrance.

Despite great advances in the knowledge of genetics in pancreatitis, currently it is advised to evaluate for mutations only in patients with hereditary pancreatitis.

Autoimmune :

Autoimmune chronic pancreatitis (AIP) is a rare but distinct form of chronic pancreatitis that is associated with autoimmune features. AIP is characterized by specific histopathologic and immunologic features. The morphologic hall marks are periductal infiltration by lymphocytes and plasma cells and granulocytic epithelial lesions with consequent destruction of the duct epithelium and venulitis.

The pathogenesis of AIP involves a cellular (CD4+ and CD8+ T cells) and humoral immune mediated attack of the ductal cells and pancreatic ducts resulting in cytokine mediated inflammation and periductular fibrosis, which leads to obstruction of the pancreatic ducts.

AIP is characterized clinically by minimal abdominal pain and diffuse enlargement of the pancreas without calcifications or pseudocysts.

On laboratory examination, these patients have hypergammaglobulinemia and autoantibodies, such as antinuclear and anti-smooth muscle antibodies.

Obstructive :

Obstruction of the main pancreatic duct is well known to result in chronic pancreatitis. The most common etiologies include scars of the pancreatic duct, tumors of the ampulla of Vater and head of the pancreas, and trauma.

Main pancreatic duct obstruction may lead to stagnation and stone formation of pancreatic juice (stone and duct obstruction theory) or acute recurrent

pancreatitis and periductular fibrosis (necrosis fibrosis theory) Histopathologic characteristics of human chronic pancreatitis resulting from obstruction include uniform distribution of interlobular and intralobular fibrosis and marked destruction of the exocrine parenchyma in the territory of obstruction, without significant protein plugs and calcifications.

Chronic pancreatitis results from plugging of the pancreatic duct. The origin of chronic pancreatitis was within the lumen of the pancreatic ductules in contrast to the origins of acute pancreatitis which tends to be inside the acinar cell. Increased lithogenicity of pancreatic fluid leads to the formation of eosinophilic proteinaceous aggregates, which precipitate and obstruct the pancreatic ductules.

Alcohol decreases the formation and the secretion of pancreatic juice, making it more viscous ; low in bicarbonate ; rich in protein, enzymes and calcium crystals ; and deficient in lithostatin.

Alcohol also has been shown to mediate the release of gastrointestinal hormones by increasing cholecystokinin releasing factor, which affects pancreatic juice formation and flow. The pancreatic stones and plugs are believed to produce ulceration of the ductal epithelial cells resulting in inflammation, fibrosis, obstruction, stasis and further stone formation.

Mechanism of chronic pancreatitis was a dysregulation and overactivity of the hepatic mixed function oxidases leading to oxidative stress. This theory places

the acinar cell at the major area of injury by oxidative stress, usually as a result of steady exposure of xenobiotics that induce the cytochrome P-450 enzymatic system, while depleting glutathione.

Pancreatitis is triggered through interference of the methionine to glutathione transsulfuration pathway, resulting in diversion of free radicals into the pancreatic tissue, with consequent activation of inflammation and fibrosis of the ductules with low flow of pancreatic juice, inhibition of lithostatin, and precipitation of proteins and calcium (Braganza 1998 ; Wilson et al, 1990). Alcohol also may contribute to increase the oxidative stress resulting from depletion of scavengers, such as selenium, vitamin E and C and riboflavin, and help to induce or propagate the damage.

Alcohol and its toxic metabolites cause accumulation of intracellular lipids and fatty acid ethyl esters, which produce damage to the acinar cell. The alterations of intracellular lipid metabolism lead to fatty degeneration, apoptosis and scarring of the pancreatic parenchyma with impairment of the pancreatic microcirculation.

It was shown that these fat cells exist in the human pancreas, can migrate into the periacinar spaces, and are activated by alcohol and acetyl aldehyde, transforming into scar producing cells. The necrosis fibrosis hypothesis views the development and course of chronic pancreatitis as a consequence of severe

pancreatitis, emphasizing that fibrosis is a late development resulting from repeated attacks of acute (alcoholic) pancreatitis, which initially lead to inflammation and necrosis.

The necrosis fibrosis hypothesis has significant supporting evidence from epidemiologic and large follow up studies, which showed that chronic pancreatitis results from recurrent attacks of acute pancreatitis.

The recurrent attacks of acute pancreatitis in hereditary pancreatitis also support the necrosis fibrosis hypothesis. One important aspect that partially negates this hypothesis is the fact that the type of fibrosis that follows acute attacks of pancreatitis involves short lived collagen type III and procollagen type IV and not the long lasting collagen types I and IV (Casini et al 2000).

The primary pathogenic factor leading to chronic pancreatitis is an outflow obstruction likely resulting from duct inflammation, destruction and fibrosis which likely are the result of an immunologic attacks on a specific genetic, structural or acquired antigen of the periductular epithelium. The target of this attack may be some specific genetic or acquired antigen on the duct epithelium.

Chronic pancreatitis seems to be an autoimmune or duct destroying disease, analogous to primary sclerosing cholangitis. The assumption is supported by several observations, such as the radiologic and histologic similarity of chronic pancreatitis and primary sclerosing cholangitis, the activation of cytotoxic

T.lymphocytes in the periductular areas of the pancreas in patients with alcoholic chronic pancreatitis, and the occasional association of chronic pancreatitis and primary sclerosing cholangitis.

The SAPE hypothesis tries to provide a “final common pathway” for the many etiologies for pancreatitis. The basic aspect is that there needs to be susceptibility (genetic or through ongoing insult, such as alcohol toxicity). The critical sentinel event appears and triggers the process causing acute and chronic pancreatitis. Further activation of the immunologic system and the stellate cells propagates chronic pancreatitis, and the end result is fibrosis and calcifications.

This hypothesis has the merits of placing several of the previous theories under “one umbrella”.

MATERIALS AND METHODS

This prospective study of chronic pancreatitis was conducted in 55 patients admitted in GRH, Madurai, General Surgery and Surgical Gastroenterology department from 2006 to 2008.

Informed consent was obtained from all patient who were included in the study.

Inclusion Criteria :

Patient with chronic pancreatitis presenting with refractory pain abdomen requiring surgical intervention were included in the study.

Exclusion criteria :

Patient with chronic pancreatitis who require surgical resection procedure are excluded from the study.

Study Design :

Each patient in the study was subjected to detailed clinical examination correlating with a detail history. Investigations in the form of routine hemogram, LFT, PFT and imaging studies like X rays, USG, CT abdomen and other investigations relevant to the suspected disease system involved were done. From the above clinical data and imaging studies chronic pancreatitis was diagnosed. Patients who requires surgical intervention were prepared and taken up for drainage procedure after satisfying the inclusion and exclusion criteria. The results were tabulated and analysed.

ANALYSIS

Age Distribution :

Table : 1

Age group	No.of cases	Percentage
1 – 10	-	-
11 – 20	16	29 %
21 – 30	14	25 %
31 – 40	12	22 %
41 – 50	10	18%
51 – 60	3	6%
Total	55	100 %

Sex Distribution :

Table - 2

Sex	No.of cases	Percentage
Male	32	58 %
Female	23	42 %
Total	55	100 %

Male : Female = 1.3 : 1

Clinical Data

Table – 3

Clinical Data	No.of cases	Percentage
Pain Abdomen	55	100%
Diabetes	18	32%
Steatorrhea	3	6%
Weight loss	14	26%
Alcoholic	15	27 %
Smoker	17	30 %
IGTT	18	32%

IGTT – Impaired Glucose Tolerance Test

Surgical Outcome :

Table - 4

Pain relief	No.of cases	Percentage
Yes	35	63.6 %
No	20	36.4 %

Clinical features- Chronic pancreatitis

Table - 5

No.of Patients	55
Mean Age	35
Sex (M : F)	1.3 : 1
Pain	100%
Diabetes	32%
Steatorrhea	6%

DISCUSSION

Age Distribution :

The youngest patient in this study was 12 years old female and oldest patient was 59 years old male. Most of the patients presented in the 2nd decade of life in this study group ie. 11 to 20 years (29%).

Sex Distribution :

Males are affected more than female patient in the ratio of 1.3: 1 in this study group.

Etiological distribution :

In this study (27%) of the patients are alcoholic. The etiological factor in this group of patients are undetermined that may be attributed to nutritional, idiopathic, hereditary etc.

Chronic alcoholism is one of the important etiological factor in chronic pancreatitis. Alcohol abuse also affects the clinical feature, course and prognosis of disease. In upto 70% of adult patient chronic pancreatitis appears to be caused by alcoholism. This form is more common in men than women between age of 30 to 40.

Hereditary pancreatitis usually begins in childhood but may not be diagnosed for several years. A determining factor is two or more family members with

pancreatitis in more than one generation.

In our series 30% of the patients were smoker. Smoking is a recognized risk factor associated with chronic pancreatitis. It also accelerates the progression of the disease. It is now recognized as an independent risk factor for chronic pancreatitis.

Idiopathic chronic pancreatitis was the most common from followed by alcoholic pancreatitis in India. **This was published by Amritha Institute of Medical Science, Cochin, India. (chronic pancreatitis : prospective nationwide study of 1086 subjects from India on Sep 2008 in pub-med.)**

Clinical Presentation :

In our study common clinical presentation was recurrent episodes of pain in epigastrium radiating to back, other features include diabetes, weight loss, steatorrhea, anorexia etc.

For most patient with chronic pancreatitis abdominal pain is the presenting symptom. Either the patient's age or the etiology of the disease has some influence in it. Most patients experience intermittent attack of pain at unpredictable intervals, while minority of patients experience chronic pain. The natural history of pain in chronic pancreatitis is highly variable.

Other symptoms include diarrhea and weight loss. This may be due either to

fear of eating (post prandial exacerbation of pain) or due to pancreatic exocrine insufficiency and steatorrhea).

A small percentage of patients (20%) have painless chronic pancreatitis, and present with signs and symptoms of exocrine and endocrine insufficiency.

Diagnosis of chronic pancreatitis :

In this study diagnosis of chronic pancreatitis is based on the thorough history, physical examination laboratory data or imaging abnormalities. Imaging methods done in this study were plain abdominal radiographs which revealed the presence of focal or diffuse pancreatic calcifications in 25 to 30% of the cases, transabdominal ultrasound which showed pancreatic duct dilatation irregularly of main pancreatic duct, loss or reduction of pancreatic parenchymal echogenicity, calculi and calcifications. CT scan abdomen findings showed pancreatic duct dilation, calcification and cystic lesions.

Imaging, modalities like ERCP and EUS are more sensitive and specific in diagnosis of chronic pancreatitis. They are expensive and the cost factor and non availability remains a constrain.

Diagnosis of chronic pancreatitis is based on a thorough history and physical examination, laboratory data and imaging studies. Today pancreatic function tests play a minor and only complementary role in the diagnosis of chronic pancreatitis.

The two main reasons for this minor role are that

- i) Non invasive test of exocrine pancreatic function show high sensitivity only in advanced stage of chronic pancreatitis.
- ii) Clinical manifestations of an exocrine pancreatic insufficiency occurs late in the course of disease after approx 90% of exocrine parenchyma is destroyed.

Exocrine pancreatic function test :

Invasive test :

1. Secretin cerulin test
2. Lundh test

Non invasive test :

1. Bentiranide test
2. PLT
3. FE – 1 (Stool test)

Endocrine pancreatic function test :

1. Fasting blood sugar
2. Oral glucose tolerance test

Imaging methods :

Non invasive imaging methods are method of choice for diagnosis of chronic pancreatitis in clinical situations. Currently ERCP is still the “Gold standard” among the all imaging methods. But in the future it may be replaced by further significant refinement of magnetic resonance imaging cholangiography.

Plain Abdominal Radiography :

Shows focal or diffuse pancreatic calcifications in 30 to 40% of cases makes the diagnosis of advanced chronic pancreatitis.

Transabdominal USG is an essential tool to visualize the entire pancreas. It is inexpensive, simple, noninvasive, widely distributed, well tolerated and often first imaging method in patient with abdominal complaint. In routine clinical situation, USG is the easiest method to detect the complication of chronic pancreatitis and to follow patients with chronic pancreatitis. Use of ultrasound for diagnosing chronic pancreatitis is limited to advanced stage.

CT scan is as specific as ultrasound but more sensitive. CT scan cannot detect early parenchymal changes and effects on small pancreatic ducts, but advanced stages and complications of the disease can be evaluated with high reliability. CT is most sensitive to detect calculi. Chronic pancreatitis is excellent method to detect advanced stage but not for early stage of chronic pancreatitis.

ERCP is still “gold standard” imaging modality. An ERCP staging system

based in pancreatic ductal changes has been developed for diagnosis of chronic pancreatitis which was published in 1984 as the Cambridge criteria. Changes of early chronic pancreatitis may not be seen on ERCP. ERCP is invasive method (post ERCP pancreatitis of 3 to 7%), expensive, specialised equipment and trained personal are necessary to perform the procedure and to interpret the pancreatograms. ERCP may be useful in distinguishing chronic pancreatitis from pancreatic cancer. The advantage of ERCP are standardization and evaluation method in multi center trials and possibility of intervention. The disadvantages are complications, costs and invasiveness.

Magnetic Resonance Imaging pancreatography an imaging method is created that enables clinicians to visualize ductal of chronic pancreatitis. The advantage of this modality is noninvasiveness. The major disadvantage is that changes of side branches are not visualized with same accuracy as in ERCP and not sensitive to detect early stages of chronic pancreatitis.

Endoscopic ultrasound visualize the pancreatic duct and the parenchyma and has the ability to detect chronic pancreatitis in patients with early stages of the disease and with advanced chronic pancreatitis. Major advantage of EUS when compared to other imaging modalities is that its ability to detect early stages of chronic pancreatitis without any complications. The disadvantage of this method is need for expert EUS endoscopist and dedicated EUS unit.

MANAGEMENT :

In this study patients with refractory intractable abdominal pain are selected and taken up for surgical drainage procedure. The most common surgical drainage procedure done was modified peustows LPJ.

The over all surgical outcome in the form of pain relief in the study group was approximately 64%. In the study group out of 55, 20 (36%) patients in the follow up period came with recurrence of pain.

The treatment of chronic pancreatitis is complex and often an interdisciplinary approach is indicated with the possibility of conservative endoscopic and Surgical therapy.

Conservative treatment :

A major component of the conservative treatment is the management of complications. This complex interaction requires individualization in nearly every case. Hence the importance of the team approach.

Pancreatic exocrine enzyme supplementation :

When weight loss or steatorrhea (15g/day) or both develop supplementation is indicated. The main goal is to ensure the optimal amounts of lipase reach the duodenum together with the delivered food. With the currently available pancreatic enzymes supplement preparation Azotorrhea can be abolished, whereas

steatorrhea can be reduced but not totally corrected. Side effects are rare except soreness of mouth, perianal irritation, abdominal pain, diarrhea, constipation, allergic reaction and fibrosing colonopathy in cystic fibrosis patient. Dose of lipase : 2500 u lipase / kg body weight per meal.

Conservative treatment of pain :

Pain significantly reduces patient's quality of life and so main goals of conservative treatment is to manage it, Medical treatment is generally the first line therapy in patients with painful chronic pancreatitis.

Alcohol abstinence and diet advice are recommended but only 50% of patients achieve pain relief.

Analgesics such as non narcotics and NSAID agents are recommended as first step. An antidepressant may have an effect on pain and increase the effect of opiates.

Interventional endoscopy and lithotripsy seems to be beneficial in cases with main pancreatic duct stenosis and obstructing calculi. Further studies are needed to evaluate the effect of pancreatic duct interventions on pancreatic pain.

About 80% of patient with chronic pancreatitis can be managed by direct recommendations and pancreatic enzyme supplements. 10 to 15% of patients need oral supplements, 5% need enteral tube feeding and approximately 1% need total parenteral nutrition. Reduction of steatorrhea and supplementation of calories are

the main goals of nutritional therapy in chronic pancreatitis. Treatment of exocrine insufficiency starts with dietary recommendations and pancreatic enzyme supplementation.

Endoscopic Treatment :

1. Decompression of pancreatic cysts by transgastric, transduodenal, and transpapillary approaches are preferred procedures in case of interventional treatment for pancreatic pseudocyst. In case of poor anatomic conditions or if there is contra indications for endoscopy patient should be referred to a surgeon.
2. Common bile duct stenting is a another indication of endoscopic intervention. A team approach between endoscopist and surgeon should guide the treatment of CBD stenosis in patient with chronic pancreatitis. The descision depends on patient age, comorbidities and cause of the stricture. Major limitations of endoscopic intervention are stent clogging, migration and cholangitis.

SURGERY :

The surgical treatment of chronic pancreatitis is based on two main concepts. Preservations of tissue via drainage operation is the goal for protection against further loss of pancreatic function. Resective procedures are performed in the case

of a non dilated pancreatic duct, if the pancreatic head is enlarged or if a pancreatic carcinoma is suspected in addition to chronic pancreatitis.

Drainage procedure :

Pancreatic duct spinceterotomy was one of the first surgical procedures proposed for patient with chronic pancreatitis and (stenosis) at the papilla of vater. This procedure was recognized as a dangerous approach and lower success rates for amelioration of pain.

More successful in patient with chronic pancreatitis and with dilated pancreatic duct is the original Puestow procedure or its modification by Partington and Rochelle. The procedure include resection of the tail of pancreas followed by a longitudinal incision along the body of the pancreas and an anastomosis with a Roux en Y loop of jejunum. The modification of Partington and Rochelle is the elimination of the resection of the pancreatic tail. Patient with a dominant mass in the head of the pancreas and a dilated pancreatic duct do not profit from a drainage procedure only. In addition to the drainage approach Beger and Izbicki proposed excavation of the head of the pancreas or the V shaped exacavation of the body along the main pancreatic duct followed by a pancreatico jejunostomy.

Resection procedures :

Whipple's procedure, Pylorus preserving pancreatico duodenectomy, Beger procedure, Berne modification of the Beger procedure (DPPHR) are the various resection procedures with merits and demerits.

Beger's procedure (DPPHR) preserved the duodenum when compared to the Whipple's procedure, which was the standard procedure in patients with chronic pancreatitis for a long time. Patients who underwent Beger Procedure had greater weight gain, better glucose tolerance and high insulin secretion capacity. Improved pain status, lower frequency of acute episodes of chronic pancreatitis, rate need for further hospitalization, low early and late mortality rates and restoration of quality of life, DPPHR seems to be able to delay the natural course of the chronic pancreatitis.

Frey procedure which involves local pancreatic head excision combined with longitudinal pancreatico jejunostomy can be considered as a standard procedure in chronic pancreatitis and has undergone evaluation in multiple trials, confirming its effectiveness as a surgical procedure for chronic pancreatitis.

Pancreatic left resection and central pancreatectomy (segmentectomy) in chronic pancreatitis are procedures which further studies to prove the effectiveness in chronic pancreatitis.

Laparoscopic Surgery :

Laparoscopic surgery can be performed successfully to manage patients

with distal chronic pancreatitis and patients with pancreatic pseudocyst. Analysis of literature suggests that laparoscopic resection of the left part of pancreas, when indicated in selected groups, produces excellent results, pain relief was achieved in 72% of patients. Laproscopic intraluminal cystogastrostomy and laproscopic anterior cystogastrostomy are safe and effective methods to treat symptomatic large pseudocyst (> 6cm in diameter)

Definite evidence from large RCT or meta analysis is still missing regarding which surgical regimen is superior in patient with chronic pancreatitis. Many still unresolved questions in the surgical treatment of chronic pancreatitis have to be answered in future randomized controlled trails.

CONCLUSION

In this prospective study which was conducted in 55 patients with chronic pancreatitis at GRH, Madurai between 2006 to 2008, the following conclusions were derived out.

1. Most of the patients presented in their 2nd decade of life and mean age is 35.
2. Males are affected more than females in the ratio of 1.3 : 1
3. In this study 27% of the patients are alcoholic the etiological factor in this group of patients are undetermined, that may be attributed to Nutritional, Idiopathic, hereditary etc.
4. Recurrent episodes of pain in epigastrium radiating to back is the most common presentation in this study group. Other features include diabetes, weight loss, anorexia steatorrhea etc.
5. Modified Puestow's is the most commonly performed surgical drainage procedure and has good results in pain relief post operatively to 64% in this study group.

PROFORMA

Name : _____ **Age / Sex :** _____

Place : _____ **Ward :** _____ **IP No.** _____

Clinical Data :

1. Abdominal pain
2. Diabetes
3. Steatorrhea
4. Loss of weight
5. Jaundice
6. Physical findings

Epigastric tenderness

Epigastric Mass

Hepatomegaly

Ascites

Investigations :

1. Blood – Sugar, Urea, Creatinine
2. Serum Amylase, lipase
3. Oral glucose tolerance test
4. Haemogram
5. Liver function test

6. pancreatic function test

Imaging

1. Plain X ray – abdomen
2. Ultra sound – abdomen
3. CT Scan – abdomen
4. ERCP
5. MRCP

Treatment

Surgery – Drainage procedure

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